



Big Data Benefits for Terminal Cancer Patients

By: Orna Feldman

A spiral of disease, debilitation and death confronted Krista Coleman when she was 26. Her uncle, who had been recently diagnosed with glioblastoma, an aggressive brain cancer, came to live with her, her 87-year-old grandmother, and another family member. Intense emotional unpredictability was their collective experience: Her uncle's erratic behavior; overwhelming confusion; medication non-compliance, and declining mental and physical competence created continually-changing minefields they had to navigate together as a family. "It was a horrible, heartbreaking experience, like a hurricane," says Coleman, a research development specialist at Harvard T.H. Chan School of Public Health. For Coleman and tens of thousands of others, "information and counseling about end-of-life care options at the time of diagnosis would have helped enormously."

However, the dearth of outcomes research on terminal brain cancer is pronounced. Filling the research gaps could dramatically help physicians, patients, families and other caregivers make better-informed end-of-life decisions, enhance patients' quality of life, reduce unnecessary hospital admissions and potentially improve resource allocation.

Entering the fray is a physician/researcher duo: radiation oncologist Nils Arvold, formerly at Dana Farber Cancer Institute and now at University of Minnesota's St. Luke's Cancer Center, and Francesca Dominici, professor of biostatistics and senior associate dean for research at the Harvard Chan School, and their respective teams.

Their collaboration, novel in the neuro-oncology sphere, unites clinical expertise and comparative effectiveness research, conducted with innovative statistical methodology, to improve quality of life for elderly patients with glioblastoma.

INNOVATIVE METHODOLOGY

Randomized prospective trials, considered the gold standard for clinical research, present limitations in neuro-oncology: With strict eligibility requirements, they involve a small number of patients—many relatively healthy—and typically don't focus on the elderly.

Comparative effectiveness research, on the other hand, gathers retrospective evidence from real-life medical outcomes. With a lens on harms and benefits of different treatment options, the methodology assesses the impact of drugs, devices, tests, surgeries, and a host of other factors. The need for hard data on these issues dovetails with neuro-oncology's rising interest in terminal patients' quality of life.

Arvold brings his knowledge of diagnoses, treatments, nuances of disease palliation and emerging trends in cancer management. With the methodology she and her team developed, Dominici brings raw computational power, which speeds big-data analyses, and innovative statistical modeling, which controls for an array of biases.

The data are messy. Potential confounders include age, severity of disease, co-existing medical conditions, access to care,

poverty, race and myriad other factors. The richness of the data—based on a registry covering 28% of the US population, as well as 14 million Medicare claims—enables Dominici to validly match data among comparable groups and then pinpoint specific variables to assess the impact of each.

"The existing research literature is rigorous but may not be relevant to specific challenges I face daily with my glioblastoma patients," explains Arvold. "A clinical trial may show chemotherapy will extend by three months the life of a 42-year-old with relatively good health. But I may be treating a 75-year-old man with seizures and confusion, the sort of patient who has not been well-represented in prior studies." Citing the frequent divide between statistical research and clinical care, Dominici points to the value of their joint effort: "Without Nils, I wouldn't have any idea which questions are best to look at. I could work for years and in the end it wouldn't be helpful to clinicians. Above and beyond developing a rigorous theory and analysis, I want my research to be impactful. Only by working together can we get a fuller picture."

EDUCATIONAL DIMENSION

To extend the collaboration's real-world benefit, several statistical graduate students were integrated into the project. For Matt Cefalu, then Dominici's post-doctoral fellow and now a statistician at the RAND Corporation, "conducting an analysis for oncologists who will make treatment decisions based on the results is very com-

elling. That real-world impact is one of reasons why I ended up at RAND, where everything is aimed at informing policy.” Working on the project offered him an additional benefit: “It improved my communication with non-statisticians. Explaining the underlying data analysis to others is an important skill for me. I work on interdisciplinary teams and communicating effectively across disciplines is essential.”

QUESTIONS LOOKING FOR ANSWERS

Gathering baseline data, the team first explored the frequency and length of time elderly glioblastoma patients spend in the hospital. The median survival from diagnosis to death is about five months, their research found—a dramatic study in contrast to survival for breast and other cancers. In addition, “a large number of patients were hospitalized for a strikingly high proportion of the rest of their lives,” reports Arvold. More than one in five spent at least 30 days in the hospital between being diagnosed and dying; an even greater number spent at least one-quarter of their remaining lives as inpatients. Given the devastation wrought by the disease, patients’ short survival, and the commonly-held view that hospitals are the worst place for terminal patients to be for quality of life, “we should investigate how to make their end of life more comfortable,” Arvold says. Strategies to reduce or avoid hospitalization and improve patients’ quality of life, the study concluded, are urgently needed.

Another of their studies, under review, looks at best treatments for elderly glioblastoma patients. Current standards of care are based on 2005 research that excluded patients 70 years and older. Since at least half of all glioblastoma patients are 65 plus—often with other conditions and greater complications than younger patients—current guidelines don’t address the best treatment for a large swath of patients.

The 2005 study found that adding a chemotherapy called temozolomide to the treatment regimen significantly prolongs life in the younger group. Arvold and Dominici are asking a question never before asked: Will adding the chemotherapy also prolong life for older people with termi-

nal brain cancer? The answer is again yes, though minimally.

Arvold/Dominici’s third study, in progress, focuses on the impact palliative care has on medical resource use among advanced brain, lung, pancreas, and colon cancer patients. Exploring end-of-life hospitalizations, emergency room visits, chemotherapy treatments, hospice enrollments and other medical actions also offers indirect quality-of-life data critical to optimal care. If, for example, the study finds palliative care is associated with fewer hospitalizations and the burdens they bring, without shortening survival, the ramifications for terminal patients’ quality of life and the healthcare system would be significant.

END-OF-LIFE CONVERSATIONS: TO HAVE OR NOT TO HAVE?

Relevant to these projects’ results are end-of-life conversations with terminal patients. “While our research doesn’t explore these conversations specifically,” says Arvold, “all three projects highlight the importance of end-of-life conversations. There’s often a resistance among neuro-oncology patients and physicians to talk early on about end-of-life. But survival is typically short and these conversations are a crucial next step.”

Radiation oncology nurse Rachel Silverman, who works with Arvold, has 25 years experience engaging in, and witnessing end-of-life conversations with advanced cancer patients. “Doctors aren’t always ready to say to the family—‘Let’s explore where the disease is going,’” Silverman says. Though comfortable discussing palliative care options with patients, she takes the doctor’s lead in broaching the subject with them.

When patients and families face a glioblastoma diagnosis, she says, “they’re focused on survival, on beating the curve. Rarely do they fully consider quality of life; they’re thinking about the extra millimeter of life, or about a miracle.” Silverman says the American mindset promotes these attitudes: “We have a culture of the denial of death. In the land of everything, there’s always something else.”

Avoiding these end-of-life conversations “closes people’s ability to make important life choices about their care and how they

want to live their lives,” Silverman says. By contrast, having these conversations, where the team can openly acknowledge the patient’s life-limited situation, “would be better for patients. It would be like we opened up the doors and sunshine and air came through. I can speak for my nursing sisters and brothers—we all feel the same weight.”

Research spearheaded by the Arvold/Dominici team strengthens the call to integrate Silverman’s approach into management early on. “If you don’t talk with patients about their end-of-life wishes,” adds Arvold, “it’s more likely they’ll end up receiving medical care, such as chemotherapy or hospitalization, which they may not prefer and which may diminish their quality of life.” Using big data, he and Dominici are helping define the optimal balance between treatments and quality of life for elderly cancer patients, enabling scores of people on all sides of the sick bed make potentially difficult decisions with less discomfort and more confidence.

